NOT FOR PUBLICATION

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

HOFFMANN-LA ROCHE INC., Plaintiff, v. APOTEX INC. and APOTEX CORP., Defendants.	Civil Action No. 07-4417 (SRC) (MAS) Civil Action No. 08-3065 (SRC) (MAS) Civil Action No. 08-4053 (SRC) (MAS) (consolidated with 07-4417 for all purposes) **OPINION**
HOFFMANN-LA ROCHE INC., Plaintiff, v. DR. REDDY'S LABORATORIES, LTD. and DR. REDDY'S LABORATORIES, INC., Defendants.	Civil Action No. 07-4516 (SRC) (MAS) Civil Action No. 08-3607 (SRC) (MAS) Civil Action No. 08-4055 (SRC) (MAS) (consolidated with 07-4516 for all purposes)
HOFFMANN-LA ROCHE INC., Plaintiff, v. COBALT PHARMACEUTICALS INC., and COBALT LABORATORIES, INC., Defendants.	Civil Action No. 07-4539 (SRC) (MAS) Civil Action No. 07-4540 (SRC) (MAS) Civil Action No. 08-4054 (SRC) (MAS) (consolidated with 07-4539 for all purposes)

HOFFMANN-LA ROCHE INC., Plaintiff, v. ORCHID CHEMICALS & PHARMACEUTICALS LTD., ORCHID HEALTHCARE, ORCHID PHARMACEUTICALS INC., and ORGENUS PHARMA INC., Defendants.	Civil Action No. 07-4582 (SRC) (MAS) Civil Action No. 08-4051 (SRC) (MAS) (consolidated with 07-4582 for all purposes)
HOFFMANN-LA ROCHE INC., Plaintiff, v. GENPHARM INC. and GENPHARM, L.P., Defendants.	Civil Action No. 07-4661 (SRC) (MAS) Civil Action No. 08-4052 (SRC) (MAS) (consolidated with 07-4661 for all purposes)

CHESLER, U.S.D.J.

This matter comes before the Court on the applications by Plaintiff Hoffman-La Roche Inc. ("Roche") and Defendants Cobalt Pharmaceuticals Inc. and Cobalt Laboratories, Inc. (collectively, "Cobalt"), Apotex Inc. and Apotex Corp. (collectively, "Apotex"), Dr. Reddy's Laboratories, Ltd. and Dr. Reddy's Laboratories, Inc., Orchid Chemicals & Pharmaceuticals Ltd., Orchid Healthcare, Orchid Pharmaceuticals Inc., and Orgenus Pharma Inc., Genpharm Inc. and Genpharm, L.P., for claim construction to resolve disputes over the construction of claim terms in U.S. Patent Nos. 4,927,814 (the "'814 patent"), 7,192,938 (the "'938 patent"), and 7,410,957

(the "'957 patent").[1]

BACKGROUND

This matter involves several Hatch-Waxman actions for patent infringement. The cases have been consolidated for pretrial purposes and arise from the following facts. Briefly, Roche owns the '814, '938, and '957 patents, which are directed to compounds and treatment methods associated with Roche's osteoporosis drug Boniva®. Defendants are generic pharmaceutical manufacturers who have filed Abbreviated New Drug Applications seeking FDA approval to engage in the manufacture and sale of generic versions of Boniva® prior to the expiration of the Roche patents.

ANALYSIS

The briefing in this case has challenged the Court to ascertain with clarity the actual disputes over claim construction. The parties appear to have written the opening briefs without a clear idea of what issues were in dispute, and these briefs manifest significant uncertainty on this score. This produced reply briefs that moved only a small step closer toward identifying the issues. In the analysis that follows, this Court has attempted to discern the actual disputes over claim construction.

I. The law of claim construction

A court's determination "of patent infringement requires a two-step process: first, the

[1] Just prior to the issuance of this Opinion, Roche voluntarily dismissed all claims against Defendants Genpharm and Apotex involving the '938 patent. Counsel for Roche has advised the Court that, while this eliminates the '938 patent from the consolidated cases, and renders claim construction of terms in the '938 patent unnecessary, the majority of the claim construction issues are the same for the '957 patent. The issues addressed in this Opinion thus remain live controversies.

court determines the meaning of the disputed claim terms, then the accused device is compared to the claims as construed to determine infringement." Acumed LLC v. Stryker Corp., 483 F.3d 800, 804 (Fed. Cir. 2007). The Court decides claim construction as a matter of law: "the construction of a patent, including terms of art within its claim, is exclusively within the province of the court." Markman v. Westview Instruments, 517 U.S. 370, 372 (1996).

The focus of claim construction is the claim language itself:

> It is a bedrock principle of patent law that the claims of a patent define the invention to which the patentee is entitled the right to exclude. Attending this principle, a claim construction analysis must begin and remain centered on the claim language itself, for that is the language the patentee has chosen to 'particularly point[] out and distinctly claim[] the subject matter which the patentee regards as his invention.'

Innova/Pure Water, Inc. v. Safari Water Filtration Sys., 381 F.3d 1111, 1115-1116 (Fed. Cir. 2004) (citations omitted).

The Federal Circuit has established this framework for the construction of claim language:

> We have frequently stated that the words of a claim 'are generally given their ordinary and customary meaning.' We have made clear, moreover, that the ordinary and customary meaning of a claim term is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application. The inquiry into how a person of ordinary skill in the art understands a claim term provides an objective baseline from which to begin claim interpretation. . .
>
> In some cases, the ordinary meaning of claim language as understood by a person of skill in the art may be readily apparent even to lay judges, and claim construction in such cases involves little more than the application of the widely accepted meaning of commonly understood words. In such circumstances, general purpose dictionaries may be helpful. In many cases that give rise to litigation, however, determining the ordinary and customary meaning of the claim requires examination of terms that have a particular meaning in a field of art. Because the meaning of a claim term as understood by persons of skill in the art is

> often not immediately apparent, and because patentees frequently use terms idiosyncratically, the court looks to those sources available to the public that show what a person of skill in the art would have understood disputed claim language to mean. Those sources include the words of the claims themselves, the remainder of the specification, the prosecution history, and extrinsic evidence concerning relevant scientific principles, the meaning of technical terms, and the state of the art.

Phillips v. AWH Corp., 415 F.3d 1303, 1312-1314 (Fed. Cir. 2005) (citations omitted).

II. Claim construction of the disputed terms in the '814 patent

The parties dispute terms in three claims of the '814 patent:

> 4. The diphosphonate compound of claim 1 designated 1-hydroxy-3-(N-methyl-N-pentylamino)-propane-1,1-diphosphonic acid and the physiologically active salt thereof.
>
> 8. A method for the treatment or prophylaxis of calcium metabolism disturbance or disease comprising administering a pharmaceutically effective amount of at least one of the compounds designated 1-hydroxy-3-(N-methyl-N-nonylamino)-propane-1,1-diphosphonic acid, 1-hydroxy-3-(N-methyl-N-pentylamino)-propane-1,1-diphosphonic acid and 1-hydroxy-3-(N-isobutyl-N-methylamino)-propane-1,1-diphosphonic acid.
>
> 12. A pharmaceutical composition for the treatment or prophylaxis of calcium metabolism disturbance or disease containing an effective amount in a pharmaceutically acceptable carrier of at least one compound designated 1-hydroxy-3-(N-methyl-N-nonylamino)-propane-1,1-diphosphonic acid, 1-hydroxy-3-(N-methyl-N-pentylamino)-propane-1,1-diphosphonic acid, and 1-hydroxy-3-(N-isobutyl-N-methylamino)-propane-1,1-diphosphonic acid.

A. Construction of "1-hydroxy-3-(N-methyl-N-pentylamino)-propane-1,1-diphosphonic acid"

The parties dispute the meaning of the phrase "1-hydroxy-3-(N-methyl-N-pentylamino)-propane-1,1-diphosphonic acid," which appears in claims 4, 8, and 12.[2] This dispute is not about the complex particulars of the chemical structure

[2] For readibility, this phrase will be abbreviated as "NMNP."

of NMNP. Rather, the dispute is simply about whether NMNP includes or excludes the salt form of the acid. Apotex and Cobalt propose that this phrase is limited to the chemical in free acid form only, whereas Roche proposes that it does not exclude salt forms of the acid.

In its initial claim construction brief, Roche asserts that NMNP would be understood by one skilled in the art as ibandronic acid. Roche then contends that claim four, which expressly includes the salt form of NMNP, does not exclude salt forms. This states the obvious and does nothing to support the contention that NMNP does not exclude salt forms.[3]

In its reply brief, Roche significantly modifies its assertion that NMNP means ibandronic acid, adding that one skilled in the art would understand that an acid can exist in different forms, such as the free acid, zwitterion, and anion forms. Roche contends that this is evidenced by the specification and the prosecution history. Yet the specific examples Roche points to are neither illuminating nor persuasive. Roche first points to this statement in the specification: "The free diphosphonic acids of general formula (I) can be isolated as the free acids or in the form of their mono- or dialkali metal salts." '814 Patent col.5 l.67 - col.6 l.1. Roche notes that this shows that the inventors did contemplate that free acids could be isolated; this appears to be correct, but Roche does not explain how this supports understanding the word "acid" to refer to chemicals in different forms. Rather, it appears to support the idea that the result of applying an isolation process to a free acid may be either a free acid or a salt. This does not support the contention that one of skill in the art would understand the word "acid" to include the salt form. Instead, as is

[3] Moreover, as will be discussed further below, the implication of this language in claim 4 is that the inventor considered NMNP to exclude salt forms, since it would otherwise have been both redundant and unnecessary to claim both NMNP "and the physiologically active salt form thereof."

discussed below, this specification statement distinguishes an acid from a salt.

Roche next asserts that "the inventors clearly and explicitly state in their specification that the compounds claimed should not be construed as limited to any particular connotation," but should be understood to include all compounds which can be derived by combination of all the meanings in the claims. There are two problems with this position. First, the statement in the specification (col. 6 ll.43-48) on which Roche relies does not say what Roche says; it is preamble language to a list of preferred compounds. Second, Roche's point appears either trivial – claims should be construed as broadly as their scope allows – or incorrect, if Roche is suggesting that the specification should be used to broaden claim scope beyond what is written in the claims: the specification cannot be used to read express limitations out of claims. See Texas Instruments v. United States ITC, 988 F.2d 1165, 1171 (Fed. Cir. 1993) (rejecting a claim construction that "would read an express limitation out of the claims.")

Roche then points to the list of preferred compounds in the specification and notes that not one of the compounds is described as a free acid, nor are ionic forms of acids excluded. This does not appear to give support to Roche's position in any way.

Lastly, Roche points to the testimony of its experts. Yet, the statements of the experts that Roche proffers do not make its case. Roche argues that:

> By definition, depending on the environment, "acids" donate protons (i.e., hydrogens) and are in a state of flux as the protons (i.e., hydrogens) move from one molecule or location to another. For instance, if ibandronic acid were in solution as it would be in an *in vivo* environment, it would be expected to convert from one form into another and back again – and quite rapidly. In an acidic environment, at any given moment, some of the ibandronic acid molecules will be in 'free acid' and zwitterion forms and some will be in ionic or anion (negatively charged) form.

(Roche Reply Br. 23.) Notice the qualification inherent in every statement: the property of being in a state of flux as to form is connected to the environment the acid is in. The relevant claim language contains no such references to the environment or to ibandronic acid being in solution. Notably, Roche does not contend that it is an inherent characteristic of ibandronic acid that its form oscillates between acid and salt. The fact that in certain situations – situations which Roche has not shown are either stated or implied by the claim language – the form of ibandronic acid oscillates between acid and salt says nothing about the meaning of NMNP in the claims.

In sum, not one of Roche's claim construction arguments about the meaning of NMNP is persuasive. Apotex and Cobalt, on the other hand, make a number of persuasive points, all along the lines of pointing out that several claims expressly distinguish the acid form and the salt form, as does the specification, which requires the conclusion that the inventors did not see the acid form as including the salt form. The claims expressly identify NMNP as an acid, and claims 3, 4, and 5 all identify a disphosphonic acid and follow the acid with the phrase "and the physiologically active salt."[4] The only reasonable way to understand this language is that the specified diphosphonic acid does not include the salt form; if it did include the salt form, it would be redundant to add the phrase "and the physiologically active salt."

Apotex and Cobalt also observe that claims 8 and 12 refer to NMNP but do not add the phrase "and the physiologically active salt." Apotex and Cobalt argue persuasively that the presence and absence of this phrase should be construed as both meaningful and limiting, and that claims 8 and 12 should be construed as excluding the salt form.

Apotex and Cobalt then note several examples of language in the specification that

[4] Claims 3 and 4 add "thereof" after "salt," while claim 5 does not.

support their assertion that the inventor clearly differentiated between the free acid and salt forms.[5] The Court need not discuss every example offered by Apotex and Cobalt. As discussed above, the language in the specification is consistent with the language in the claims and clearly differentiates between free acids and salts.

Having examined the language of the claims and of the specification, this Court concludes that Apotex and Cobalt are correct, and that the claim term "1-hydroxy-3-(N-methyl-N-pentylamino)-propane-1,1-diphosphonic acid" excludes the salt form of the acid.

B. Construction of "physiologically active salt"

Apotex and Cobalt propose that the phrase "physiologically active salt," appearing in claim 4, should be construed to mean: "A solid substance in which the salt ion provides its own active effect, separate and apart from any drug component that may be included as an anion within the final salt product." Roche proposes that this phrase should be construed to mean: "a salt form of ibandronic acid that is physiologically active, i.e., capable of producing physiological activity."

In short, Apotex and Cobalt's argument consists of these statements: "A person of ordinary skill in the art would recognize that the term 'physiologically active' when applied to the term 'salt' requires a salt component that itself produces an intended physiological effect,

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[5] For example, Apotex and Cobalt point to the statements in the specification which discuss the preparation processes that have been disclosed. '814 Patent col.4 ll.34-47. In brief, the specification states that a tetraester may be saponified to a free acid of formula (I), and that such compounds may be converted into "their pharmacologically compatible salts." '814 Patent col.4 ll.43-47. This clearly implies that free acids and salts differ, and that a conversion process is required to change one into the other.

separate and apart from any effect caused by the drug component itself (here ibandronate). . . [A] physiologically active salt is a solid product in which the salt cation has activity additional to that provided by the drug anion with which it is associated in a solid." (Apotex and Cobalt Br. 16.)

There are two problems with this construction. First, solely as a matter of the plain language, Apotex and Cobalt does not explain why "physiologically active salt" should require that both the anion and the cation components show independent physiological activity. Apotex and Cobalt state that ibandronate sodium is a salt because it is a solid product which consists of an ibandronate anion and a sodium cation. (Apotex and Cobalt Br. 15.) From the standpoint of ordinary meaning, it would appear that a "physiologically active salt" should be a salt that is physiologically active. Yet Apotex and Cobalt contend that it should be understood as requiring more, as requiring separate physiological activity from both the anion and the cation. The plain language does not suggest this. Apotex and Cobalt's proposed construction adds in claim limitations with no basis in the ordinary meanings of the words.

A second problem with this construction is that it appears to be disconnected from the '814 patent and what the inventor invented. The patent is directed to the part of the salt molecule that is here referred to as the drug anion. There is nothing in the patent which suggests that the inventor invented a combination molecule in which the anion and cation each were independently physiologically active.[6]

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[6] In Phillips, the Federal Circuit instructed courts to consider what the inventor actually invented. The Court quoted Renishaw PLC v. Marposs Societa' per Azioni, 158 F.3d 1243, 1250 (Fed. Cir. 1998)), as follows:

> Ultimately, the interpretation to be given a term can only be determined and confirmed with a full understanding of what the inventors actually invented and intended to envelop with the claim. The construction that stays true to the claim

The difficulty with this proposed construction becomes more apparent when one looks to the statement in the expert report of Dr. Gould which Apotex and Cobalt cite in support: "I would interpret this meaning that the salt cation acts as a drug in its own right offering therapeutic benefit *in addition* to that provided by moiety [sic] that is the counterion." (Hunt Decl. Ex. 11 ¶ 81.) Thus, Dr. Gould is proposing that the phrase at issue requires a double-acting combination drug, a molecule in which the two component parts have separate therapeutic actions. As just stated, there is nothing in the patent that suggests that the inventors thought they had invented a double-acting combination drug.

There is no dispute about what the word "salt" means here. Nor is there any dispute about what "physiologically active" means. Roche has correctly construed the phrase to mean a salt of ibandronic acid that is physiologically active.

C. Construction of "calcium metabolism disturbance or disease"

The parties assert that they dispute the meaning of the phrase "calcium metabolism disturbance or disease," which appears in claims 8 and 12. Claim 8 is directed to a method for the treatment or prophylaxis of calcium metabolism disturbance or disease, and claim 12 is directed to a pharmaceutical composition for the treatment or prophylaxis of calcium metabolism disturbance or disease.

In its opening brief, Roche asserted that it was relying on Apotex and Cobalt's statement that they did not dispute Roche's proposed definition (which was, in short, that the phrase meant

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> language and most naturally aligns with the patent's description of the invention will be, in the end, the correct construction.

Phillips, 415 F.3d at 1316.

what it said). In their opening brief, however, Apotex and Cobalt argued that the phrase should be construed to exclude post-menopausal osteoporosis. In its reply brief, Roche argued that the claim language does not exclude any particular type of osteoporosis.

Having considered the parties' briefs, this Court find no active controversy about the construction of this claim language. There are no disputes about the meaning of the phrase "calcium metabolism disturbance or disease."[7] Rather, the parties dispute the factual question of whether post-menopausal osteoporosis is, in fact, a calcium metabolism disturbance. The parties muster the opposing opinions of experts, as well as other kinds of scientific evidence, on this factual, medical question.[8] This factual inquiry belongs to the infringement analysis, and is a matter for resolution on summary judgment or at trial.

D. Construction of "administering"

The parties dispute the meaning of the word "administering" in claim 8. Apotex and Cobalt maintain that "administering" requires the direct administration of the acid to the patient. Roche contends that "administering" includes situations in which a non-acid form is given to the patient, enters the body, and is converted by the patient's body into an acid form. This dispute has significance because Roche contends that Defendants' product, ibandronate sodium, which is

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[7] The parties have not focused on the issue of whether these phrases which state intended use are claim limitations. The question of whether a statement of intended use operates as a claim limitation is often litigated. See, e.g., Bicon, Inc. v. Straumann Co., 441 F.3d 945, 952 (Fed. Cir. 2006). In its opening brief, Roche contends that these are statements of the purpose of the invention, but, in the responsive briefs, all the parties argued as if these phrases stating intended use are claim limitations.

[8] Roche also points to the definition of "osteoporosis" in the medical inquiry, and claims that this is extrinsic evidence. The problem is that "osteoporosis" is not in the claim language. This is not extrinsic evidence of the meaning of disputed claim language. See Phillips, 415 F.3d at 1322. It is, rather, evidence relevant to the infringement inquiry.

not in a free acid form when it sits in the pill, gets converted into the acid form when it is inside the body.

"[T]he words of a claim are generally given their ordinary and customary meaning . . . [T]he ordinary and customary meaning of a claim term is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention." Phillips, 415 F.3d at 1312-13 (citation omitted). Thus this Court begins the claim construction inquiry by asking whether a person of ordinary skill in the art would have understood "administering" in a way that differs from the ordinary and customary meaning of the word.

In its opening brief, Roche states: "[t]he term 'administering' has its ordinary meaning." (Roche Br. 19.) In that brief, Roche does not elaborate on or qualify this contention. In its reply brief, Roche suddenly – and without explanation – takes an entirely different position: "'administration' of a biphosphonate encompasses the entire process by which the drug travels through the gastrointestinal tract and flows through the body via the bloodstream to reach its intended destination of therapeutic activity, which is the surface of bone." (Roche Reply Br. 33-34.) Roche has thus abandoned its argument that "administering" has its ordinary meaning.

This Court accepts Roche's initial proposed construction and rejects its second one. The rejection of the second construction rests on two main grounds. First, as a matter of procedure, this Court will not accept arguments offered for the first time in a reply brief, as they were not properly asserted in the opening brief, and Defendants have not had the opportunity to respond to them. Anspach v. City of Philadelphia, 503 F.3d 256, 258 n.1 (3d Cir. 2007) ("failure to raise an argument in one's opening brief waives it"). Second, Roche's position relies on unpersuasive extrinsic evidence that cannot, under Federal Circuit law, be used to alter the meaning

established by the intrinsic evidence.

In support of its second construction, Roche points to two reports by its experts, Drs. Benedict and Chesnut. Dr. Benedict opines that "the administration does not end once the biphosphonate product enters the body." (Benedict Reply Rpt. ¶ 164, Dede Decl. Ex. C.) This statement of the ultimate conclusion of claim construction is a matter of law reserved for the Court. Moreover, Dr. Benedict offers neither scientific argument, nor even analysis of the patent, to support this view. Dr. Benedict does quote the relevant language in the specification, and asserts that it "conveys" to him his construction. (Id. at ¶¶ 163-164.) Without explanation, however, the quoted specification language does not persuade this Court that he is correct. Ultimately, Dr. Benedict fails to illuminate this subject beyond offering his unexplained belief that administration does not end once the drug has entered the body.

Dr. Chesnut begins his discussion of the meaning of "administering" by examining the specification and the Webster's definition, which is "to give remedially." (Benedict '814 Reb. Rpt. ¶¶ 38-39, Dede Decl. Ex. A.) Dr. Chesnut then states: "this is what a person of skill in the art would understand 'administer' to mean." (Id. at ¶ 40.) It is perplexing to consider how Roche believed that Dr. Chesnut's opinion supported Roche's position, since it appears to contradict and undermine it. The meaning "to give remedially" conflicts with Roche's contention that administering does not end until the medication reaches the bone. There is nothing in the concept of giving remedially that suggests travel through all the paths inside the body until the medication reaches its ultimate destination.

To the contrary, it would appear from this Webster's definition that administering stops when the giving stops, and the giving stops as soon as the patient has received the medication.

Does the giver continue to give while the medication gets digested and travels through the bloodstream? This Court thinks not. And "remedially" here refers to the intent of the giver while giving, and does not extend the act of giving through the entire act of remediation, which could conceivably go on for the life of the drug inside the body, however long that may be.[9]

Dr. Chesnut refers to Webster's secondary definition of "administer." The primary definition is: "to manage or supervise the execution, use, or conduct of."[10] Administering thus should last only as long as the person doing the administering is managing its execution. Once the patient's body has begun acting on the medication, the person administering is no longer managing the execution of the act of giving or the use. That is the point at which administering stops.

Roche has offered nothing to support its proposed construction of administering. Instead, Dr. Chesnut's opinion supports the conclusion that the ordinary meaning is the correct one.

Moreover, examination of the intrinsic evidence does not indicate that the patentee acted as his own lexicographer and assigned a special meaning to "administering." Although the instant dispute involves only claim 8, the Court may look to how a word is used in other claims to illuminate its meaning. Phillips, 415 F.3d at 1314 ("Because claim terms are normally used consistently throughout the patent, the usage of a term in one claim can often illuminate the meaning of the same term in other claims.") Examination of the language of claim 7 suggests that administering goes no further than the point at which the compound has entered the patient's

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[9] Cobalt states: "The drug may in fact not even begin to perform any therapeutic work until weeks and months after it was first consumed by the patient." (Cobalt Br. 26.)

[10] Merriam-Webster's Online Dictionary, http://www.merriam-webster.com/dictionary/administer (last visited April 20, 2010).

body.

Claim 6 begins with this language: "A method for the treatment or prophylaxis of calcium metabolism disturbance or disease comprising administering a pharmaceutically effective amount of . . ." This does not inform our inquiry into the point at which administering stops. Claim 7 depends on claim 6: "The method of claim 6 wherein 0.01-10 mg P/kg of the pharmaceutically acceptable diphosphonate compound are administered per day." The language of claim 7 does not support Roche's proposed construction. In claim 7, a dose of a pharmaceutically acceptable diphosphonate compound is administered. Thus, the time frame for "administered" must not conflict with the time frame for the "pharmaceutically acceptable diphosphonate compound." The time frame for the "pharmaceutically acceptable diphosphonate compound" ends when the disphosphonate compound stops being pharmaceutically acceptable, or a compound. The parties appear to agree that chemical transformations to the medication occur in the stomach. It is difficult to imagine making the case that a medication that has been subject to such transformations in the stomach is pharmaceutically acceptable. Thus, the time frame for a "pharmaceutically acceptable diphosphonate compound" certainly ends before digestion does its work. As a result, the time frame for "administering" must end earlier than digestion.

The language of the specification is consistent with this interpretation. Both parties point to this relevant language:

> The new compounds of general formula (I) according to the present invention and the salts thereof can be administered enterally or parenterally in liquid or solid form. For this purpose, there can be used all conventional forms of administration, for example tablets, capsules, dragees, syrups, solutions, suspensions and the like.

'814 Patent col.6 ll.12 - 18. Particularly persuasive is the fact that the specification states that the

compounds can be administered in solid form. Again, this suggests that administering a solid would end when the solid form itself ended. It is certainly inconsistent with Roche's proposed construction, which has administering lasting well after the solid form has ended due to digestion in the stomach. There is no way that the body's circulation of a medication through the bloodstream could be said to involve a solid form of the drug, within the meaning of "solid form," as used in the specification.

Cobalt and Apotex also point to this statement in the specification: "The dosages to be administered daily are about 1 to 1000 mg. [] and can be given once or several times per day." '814 Patent col.6 ll.39-42. This indicates that dosages are both administered and given, which supports the understanding of "administered" as being close in meaning to "given." This, in turn, supports the proposition that administering stops when the act of giving to the patient stops.

In sum, the intrinsic evidence contradicts Roche's position and supports that of Cobalt and Apotex.

Roche also argues that its proposed construction is consistent with that in Ortho-McNeil Pharm., Inc. v. Mylan Labs., Inc., 348 F. Supp. 2d 713, 730 (N.D. W. Va. 2004), in which the court construed "administering" as follows:

> Further, claim 5 discusses "administering" the levofloxacin. Daiichi/Ortho maintains that this term limits the claim to something delivered from outside the body and thereby excludes in vivo production of levofloxacin. In response, Mylan argues that if ofloxacin were to become levofloxacin in vivo, an antimicrobially effective amount of levofloxacin would have been administered when ofloxacin was administered. It therefore maintains that the language does not exclude in vivo production.
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> Mylan's construction is supported by the Merriam Webster Medical Dictionary's definition of administer, "to give remedially (as medicine)." Whether levofloxacin formed as the claimed compound inside the body or outside the body, as long as it

> is given remedially as medicine, then levofloxacin has been administered. Thus, claim 5 does not contain a preingestion limitation.

The problem for Roche is that this case relies on a dictionary definition and was decided prior to Phillips. It seems unlikely that this would still pass muster under Federal Circuit law, given the teaching of Phillips about the lesser importance of extrinsic evidence such as dictionaries in claim construction. Phillips, 415 F.3d at 1320 (disapproving the district court's claim construction because "the methodology it adopted placed too much reliance on extrinsic sources such as dictionaries . . . and too little on intrinsic sources, in particular the specification and prosecution history.")[11]

Roche has failed to persuade this Court that one of ordinary skill in the art would have understood "administering" to have an end point beyond the point at which the body transforms the medication from its initial form. Rather, the intrinsic evidence, both in the claim language itself and in the specification, shows that the patentee understood "administering" to end at the point at which the body has received the medication and begins to transform it from its initial form. This is consistent with the ordinary meaning of the word which, as Dr. Chesnut stated, is "to give remedially." In the ordinary understanding of the word, administering stops when the giving is done, which is at the point at which the patient has received the medication.

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[11] Another case cited by the parties is Schering Corp. v. Glenmark Pharmaceuticals Inc., USA, 2008 WL 4307189 at *8 (D.N.J., September 16, 2008), in which that Court construed "administering" as "to provide externally by way of ingestion." This case has little persuasive value, for two reasons. First, that Court relied heavily on the use of "administering" in the context of the words "dose" and "dosage," which do not have the same role in the relevant sections of the '814 patent. Second, the specification in the '814 patent makes clear that the patentee's concept of administering is not limited to methods involving ingestion, but is broader.

E. Construction of "pharmaceutical composition . . . containing"

The parties say that they dispute the meaning of the words "pharmaceutical composition . . . containing" in claim 12. Roche, however, has not even articulated a position about this issue, much less persuaded this Court of its merit. Roche's opening brief says that a dispute "appears to be emerging," but then gives no clear statement of this dispute and says that it will say more in its responsive brief. (Roche Br. 21-22.) In its responsive brief, Roche again does not articulate a position on the meaning of this language, but only argues against the position of Apotex and Cobalt.[12] Roche has failed to propose any construction for this particular language.

Apotex and Cobalt argue that this language requires "a tangible composition, such as a tablet or capsule, that has the free acid actually present." (Apotex and Cobalt Br. 26.) This is poorly stated, because the Court reads Defendants' position to be that the composition has the free acid present prior to the entry of the composition into the body.[13] Apotex and Cobalt then point to a variety of pieces of evidence from the specification. This evidence does not need extensive discussion. There is nothing whatever in the patent to suggest that a pill that is in the process of being digested in a patient's stomach is a pharmaceutical composition within the meaning of claim 12. The conventional understanding of "composition" is that it exists in a state

[12] The argument that Roche makes against Apotex and Cobalt's proposed construction says little. Roche observes that the specification states that the compositions for oral administration may include flavoring and sweetening agents, thus showing that the compositions would be tasted and thus would exist inside the body. Yet there is no question that the compositions will exist inside the body; a pharmaceutical effect would never occur if the compositions never entered the body.

[13] Apotex and Cobalt use the phrase "tangible composition" but seem to mean "composition existing outside the body."

in which it is mixed together.[14] When it is broken apart, as it would be during digestion, it is no longer the same composition. Having examined the specification, this Court concludes that the patentee meant "pharmaceutical composition" in claim 12 to be a composition that exists outside the body. Certainly Roche has failed to make any case to the contrary.

III. Claim construction of the disputed terms in the '938 and '957 patents

Roche has asserted four claims from the '938 patent and eight claims from the '957 patent. These are all dependent claims, and the claim terms requiring construction are found in the first claim of each patent, the relevant independent claims on which the asserted claims depend. The parties have agreed that, for the purpose of construing the claim terms presently in dispute, the first claims from the two patents are substantially similar, and a single analysis may appropriately resolve the disputes over the claim terms in the two patents.

Claim 1 of the '938 patent states:

> 1. A method for treating or inhibiting osteoporosis comprising commencing treatment by orally administering to a subject in need of such treatment, a first dose, on a single day, of a pharmaceutical composition comprising from about 100 mg to about 150 mg of bisphosphonic acid or an amount of a pharmaceutically acceptable salt thereof that is equivalent to about 100 mg to about 150 mg of said bisphosphonic acid and continuing said treatment by orally administering, once monthly on a single day, a pharmaceutical composition comprising from about 100 mg to about 150 mg of bisphosphonic acid or an amount of a pharmaceutically acceptable salt thereof that is eguivalent to from about 100 mg to about 150 mg of bisphosphonic acid.

Claim 1 of the '957 patent states:

> 1. A method for treating osteoporosis comprising commencing treatment by orally administering to a subject in need of such treatment, on a single day, a first dose

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[14] Thus, Merriam-Webster's Online Dictionary defines composition as "a product of mixing or combining various elements or ingredients." http://www.merriam-webster.com/dictionary/composition (last visited April 20, 2010).

> in the form of a tablet, wherein said tablet comprises an amount of a pharmaceutically acceptable salt of ibandronic acid that is equivalent to about 150 mg of ibandronic acid and continuing said treatment by orally administering, once monthly on a single day, a tablet comprising an amount of a pharmaceutically acceptable salt of ibandronic acid that is equivalent to about 150 mg of ibandronic acid.

A. Construction of "commencing treatment," "a first dose, on a single day," and "once monthly on a single day."

Claim 1 of the '938 patent and claim 1 of the '957 patent both refer to a treatment method comprising "commencing treatment" by administering "a first dose, on a single day"[15] and continuing the treatment by administering a dose "once monthly on a single day." The parties dispute whether "first" means first relative to an episode of treatment (Roche's construction), or first ever in a patient's lifetime (Defendants' construction).[16]

The parties agree that this question of claim construction should be resolved by looking to the prosecution history. There is no dispute about which events in the prosecution history are relevant; the question is only what these events mean for construing the claim language.

The section of the prosecution history of interest begins with the filing of the amendment of August 4, 2006. (JA R2001937-41.) As amended, claim 24 discloses a treatment method comprising a once monthly oral dose of 100 mg to 150 mg of biphosphonic acid. (JA R2001938.) In the office action of September 12, 2006, the examiner rejected claim 24 under § 103(a) as being unpatentable over the Schofield reference. (JA R2001955.)

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[15] Claim 1 of the '957 patent uses the words "on a single day, a first dose."

[16] Defendants filed two sets of claim construction briefs for the '938 and '957 patents. One set of briefs was filed by Defendants **O**rchid, **G**enpharm, **D**RL, and **A**potex, clumsily referenced here as the "OGDA Defendants." Another set of briefs was filed by Defendants Cobalt Pharmaceuticals Inc. and Cobalt Laboratories Inc. (collectively, "Cobalt.")

The examiner explained his reasoning as follows. Schofield teaches a method "where the compound is administered during a loading period and a maintenance period, (see the abstract)."[17] (JA R2001955.) The examiner continued:

> In such maintenance period, the biphosphonate compound is administered orally to the subject at a dosing frequency which may be once a month. . .
>
> It should be noted that it is the administration during the maintenance period which is not patentably distinct from the presently claimed method. While Schofield et al. require that their method include a loading dosage period, such a period is excluded from the present claims.

(JA R2001955-56.)

On December 13, 2006, the applicant filed a further amendment in response to this office action. (JA R2002064.) Claim 24 was amended, and this wording was subsequently allowed and became claim 1 of the '938 patent. The applicant made these remarks:

> Despite the deficiencies of Schofield, in order to advance prosecution applicants have amended the present claims to exclude the possibility of employing a loading dose administered over 7 to 180 days, as required by the methods disclosed by Schofield to be efficacious. Claims 24 to 28 and 30 to 39 exclude a loading dose by requiring the administration of a first dose, on a single day, of a pharmaceutical composition . . . followed by monthly administration of the same.

(JA R2002069-70.) On January 16, 2007, the PTO issued a notice of allowance of the claims. (JA R2002090-93.)

At the outset, in considering the arguments of the parties, this Court does not see how the

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[17] The Schofield reference is United States Patent Application No. 20030118634. The abstract states: "The methods comprise a loading period with a biphosphonate followed by a maintenance period. The loading dose is two to twenty times per day greater than the corresponding maintenance dose." The summary of the invention explains that, "[f]or oral administration, the loading dose is administered every day or every other day whereas the maintenance dose may be administered every day, twice a week, weekly, bi-weekly, or monthly."

prosecution history refers at all to the issue of whether a dose is the first in a patient's lifetime. It is quite clear that, to overcome a rejection, the applicant amended the claim to exclude a loading dose treatment phase, thus distinguishing Schofield. The point of the amendments is to make clear that the treatment regimen has only a one-dose-monthly phase, with no loading phase. In the exchanges at issue, neither the examiner nor the applicant discussed the patient's lifetime treatment history.

The interpretive issue here concerns the frame of reference for a commencement, a beginning. A beginning is relative to its time frame of reference. Thus, when we write that we began with a good breakfast, the reader must figure out whether – among a number of possibilities – our time frame of reference is our day or our lifetime. The claim construction question is thus what one of skill in the art would understand the time frame of reference to be for the particular claims.

Defendants urge the Court to construe "commencing" in terms of a lifetime frame of reference: "the term 'commencing treatment' literally excludes *prior use* of *any* product for treating or inhibiting osteoporosis." (OGDA Defs.' Br. 12.) But Defendants do not explain why this must be so. The first page of the Order accompanying this Opinion is not the first page this Court has ever written. It is not even the first page of an Order in this case. The ordinary meaning of "first" is highly context-specific and depends greatly on the time frame of reference of those communicating. As is well-established, the applicant may act as his own lexicographer and might use "commence" and "first" to be understood within the frame of reference of a lifetime, but the proponent of such a construction must provide a basis for it. Defendants have not done so.

In their opening brief, the OGDA Defendants argue that the relationship between "commencing treatment" and "first dose" supports their interpretation: "The claim term 'commencing treatment' would be merely superfluous and would not distinguish the second phase of the two-phase treatment regiment disclosed in Schofield, if it required nothing more than administering 'a first dose' of a series of monthly doses, as Roche contends." (OGDA Defs.' Br. 12.)

Defendants' superfluity argument is unpersuasive. It is true that "commencing treatment" and "first dose" have some overlap in meaning, but the prosecution history record evidence strongly supports the theory that the applicant chose "commencing treatment" and "first dose" because this language distinguished Schofield so well. As the applicant made clear in the December 13, 2006 remarks, the amendments were made to exclude the possibility of using a loading dose. To speak of "commencing treatment" using a "first dose" of monthly doses does this very well. While the "first" in "first dose" does overlap the concept of commencement, it is additionally meaningful because it is relative to the series of doses that follow. Together, "commencing treatment" and "first dose" work to sharply differentiate the applicant's method from the Schofield method.

The superfluity argument is not meritless. The problem, though, is that the argument is too weak to support an interpretation that does not otherwise fit with the prosecution history. The fact that "commencing treatment" and "first dose" do have some overlap in meaning does not necessitate the conclusion that "commencing" should be understood to carry the meaning of an absolute lifetime first. Defendants' many pages of briefing fail to point to signals in either the patent itself or the prosecution history that would tell the reader to use the frame of reference of a

lifetime. To the contrary, signals of a lifetime frame of reference are notably absent from the language of the patent, whereas signals of a regimen frame of reference are present. The time words used in the patent are "day" and "month," which do not signal any particular link to a lifetime. In the specification, the method is termed a "regimen." See, e.g., '938 Patent col.2 l.33. Furthermore, the examiner, in the remarks made explaining the rejection in view of Schofield, referred to "administration during the maintenance period" and a "loading dosage period." (JA R2001956.) This use of the word "period" to express the time frame of reference does not invoke a lifetime frame of reference. Rather, it is consistent with the idea that the time frame of reference is the period of administration of the regimen, which might also be considered the treatment episode.

In the reply brief, the OGDA Defendants attempt to bolster the superfluity argument by contending that, under Roche's proposed construction, the claim would not exclude the method of the Schofield loading dose. This is obviously meritless. If the loading dose is administered daily or every other day, and the treatment method of the '938 patent claim 1 does is administered once monthly only, from commencement onward, claim 1 excludes the loading dose. The OGDA Defendants go so far as to assert that, under Roche's proposed construction, the claim requires only monthly dosing, "no matter what comes before . . ." (OGDA Defs.' Reply Br. 9.) The commencement language clearly requires that a loading dose cannot come before.[18]

Cobalt adds to this discussion the anchor point of diagnosis. In its opening brief, Cobalt

[18] This is within the time frame of reference of the treatment episode, not the patient's lifetime.

contends that one of skill in the art would understand that commencing a method follows the event of physician diagnosis. The problem, though, is that, even if this is correct, it does not illuminate the question of the time frame of reference.[19]

In the reply brief, Cobalt, joined by Apotex, argues that the scope of the applicant's surrender during prosecution was broader than what was necessary to avoid the prior art. Cobalt then argues that this claim language should be given an extremely narrow reading: the "on a single day" limitation means that the method is limited to monthly treatment in which the dose is administered on the exact same day of each month. This is unpersuasive. Cobalt offers no justification for the contention that "on a single day" means "on the exact same day." The ordinary meaning of "on a single day" is "on one day and not more than one day."

Even granting that the superfluity argument has some weak merit, Defendants' prosecution disclaimer argument must fail, given Federal Circuit law. As Defendants themselves point out, the relevant standard is a strict one: "Under the doctrine of prosecution disclaimer, a patentee may limit the meaning of a claim term by making a clear and unmistakable disavowal of scope during prosecution." Purdue Pharma L.P. v. Endo Pharms., Inc., 438 F.3d 1123, 1136 (Fed. Cir. 2006). Even giving Defendants' arguments the most charitable reading, Defendants have not shown that the applicant clearly and unmistakably made the disavowal they contend.

The "clear and unmistakable disavowal standard" in Federal Circuit law favors Roche's construction. The prosecution history shows that the applicant clearly and unmistakably

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[19] If anything, this merely weakens Defendants' position. Presumably, a patient receives a diagnosis on every visit to a physician – a diagnosis is, after all, something the health insurance companies demand to reimburse every visit. Thus, the event of diagnosis does little to nothing to anchor commencement to a particular time frame.

disavowed any treatment regimen which did not begin with monthly dosing.[20] This Court concludes that the claim terms in claim 1 of the '938 patent, "commencing treatment," "a first dose, on a single day," and "once monthly on a single day," and the similar terms in claim 1 of the '957 patent, should be construed to refer to the time frame of the treatment episode, not the patient's lifetime.

B. Construction of "consisting of"

The briefs make some small, unpersuasive attempts to show a dispute over the phrase "consisting of," which appears in claim 16 of the '938 patent and claim 6 of the '957 patent. At the outset, it is clear from the briefs that the parties are entirely in agreement about the meaning of this well-known term of art; Federal Circuit law on the interpretation of this phrase is well-settled. Given that, this Court is left unclear about how claim construction can be useful here. In their reply brief, the OGDA Defendants point to the issue raised by the Federal Circuit in Norian Corp. v. Stryker Corp., 363 F.3d 1321, 1331 (Fed. Cir. 2004): "while 'consisting of' limits the claimed invention, it does not limit aspects unrelated to the invention. It is thus necessary to determine what is limited by the 'consisting of' phrase." This could certainly be the starting point for an inquiry, but the parties have not sufficiently briefed this issue. Should the parties decide to fully brief this issue, they may request further claim construction. The parties are advised, however, to make sure that this inquiry relates to an actual and particularized

[20] Roche makes an additional argument in support of its position which is neither necessary to prevail nor particularly persuasive. Roche points to the statement in the specification that "treatment . . . can be improved" by use of the patented method, and argues that this implies that a patient may have undergone prior treatment. '938 Patent col.2 ll.41-43. It appears that "treatment" in this sentence refers to treatment of osteoporosis in general, not treatment of any particular patient.

controversy.

This admonition arises because, aside from the Norian analysis, it appears that the parties here are urging the Court to perform speculative, on-the-fly infringement analyses for hypothetical treatments – such as "the claimed once-per-month dose of oral ibandronate in combination with (before, after or concurrently with) any non-biphosphonate, such as products containing calcium and/or vitamin D, for treating or inhibiting osteoporosis." (OGDA Defs.' Br. 17.) The Federal Circuit has cautioned that claim construction that is not performed in the context of a particular infringement dispute runs the risk of bring "something akin to an advisory opinion on the scope" of the patent. Lava Trading, Inc. v. Sonic Trading Mgmt., LLC, 445 F.3d 1348, 1350 (Fed. Cir. 2006). In the absence of any actual question about the meaning of "consisting of," the Court declines to speculate about whether hypothetical treatments would or would not be excluded, and thus, noninfringing.[21]

C. Construction of "continuing said treatment"

Cobalt contends that the phrase "continuing said treatment" in claim 1 of the '938 patent and claim 1 of the '957 patent is indefinite, and that one of skill in the art would lack any guidance about what continuing said treatment would mean. This is meritless. Viewed as a whole, the briefs make clear that no one has any genuine uncertainty about the method at issue here, which is once-monthly administration of a particular medication. Although Cobalt contends that there are multiple possibilities for interpretation, Cobalt fails to point to any

[21] Similarly, Cobalt and Roche dispute the question of whether "orally administering to a subject in need of such treatment" requires one person or two, but do not explain how this point is material. In light of Lava Trading, this Court will not construe claims without the context of an actual infringement dispute needed to make the interpretive process meaningful.

alternative meanings, aside from the obvious one. Cobalt has failed to persuade that the meaning of that phrase is indefinite.

This Court finds in the briefs no other question as to the meaning of "continuing said treatment."

CONCLUSION

This Court has examined the disputes over claim construction raised by the parties. As to the '814 patent, the disputes are resolved as follows: 1) the claim term NMNP excludes the salt form of the acid; 2) "physiologically active salt" means a salt of ibandronic acid that is physiologically active; 3) "administering" stops at the point at which the patient has received the medication; and 4) "pharmaceutical composition" means a composition that exists outside the body. As to the '938 and '957 patents, the Court concludes that the claim terms in claim 1 of the '938 patent, "commencing treatment," "a first dose, on a single day," and "once monthly on a single day," and the similar terms in claim 1 of the '957 patent, should be construed to refer to the time frame of the treatment episode, not the patient's lifetime.

s/ Stanley R. Chesler
Stanley R. Chesler, U.S.D.J.

Dated: May 7, 2010